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| EXAMINER | |
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| WESTERBERG, NISSA M | |

| ART UNIT | PAPER NUMBER |
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| 1618 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/800,984 | MULYE, NIRMAL | |
| | Examiner | Art Unit | |
| | NISSA WESTERBERG | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 March 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *38,40-48,54-56,59,60 and 63-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,40-48,54-56,59,60 and 63-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Arguments*

1. Applicants' arguments, filed March 14, 2011, with respect to the pending claims have been considered but are moot in view of the new ground(s) of rejection. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

### *Claim Rejections - 35 USC § 103*

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 38, 40 – 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shell et al. (US 6,340,475) in view of Seroff et al. (US 6,387,403).

Shell et al. discloses compositions wherein drug release is accomplished by the imbibition of water by hydrophilic polymers (abstract). The formulations take the form of particles, tablets or particles retained in capsules (col 9, ln 61 – 62), all of which read on solid oral dosage forms. The water-swellable polymers can be a variety of materials, including a variety of celluloses, including microcrystalline cellulose, starch and starch-based polymers (col 7, ln 62 and 65 - 66), and the cellulose polymers hydroxymethyl-cellulose, hydroxyethyl cellulose, HPMC and carboxymethyl cellulose (col 8, ln 15 – 17). Both hydroxy ethylcellulose and HPMC are particularly preferred as the cellulose polymer (col 8, ln 23 – 25). The polymers can be used individually or in combination as certain combinations will often provide a more controlled release of drug than the components when used individually, such as cellulose-based polymers with gums (col 9, ln 42 – 48). Drug, polymer and stearate are compressed into pellets (col 12, ln 17 – 18), which reads on the mixture in the core required by the instant claims. For example, in example 6 the samples represented by open triangles are a combination of hydroxyethylcellulose (a cellulose ether) and xanthan gum (1:1 ratio; col 15, ln 16 – 21). Among the drugs that are highly water soluble which would benefit from being released in a controlled manner is metformin hydrochloride (col 7, ln 39 – 41).

Shell et al. does not disclose the inclusion of maltodextrin in the composition.

Seroff et al. discloses dosage forms in which a drug is mixed with excipients that provide an osmotic activity gradient that drives fluid from the external environment to form a deliverable drug formulation by imbibition of fluid (col 7, ln 56 – 62). In addition to a drug carrier, osmotically active agents ("osmagents"), lubricants and binders can also be included (col 7, ln 62 – 66). A layer generally comprising one or more osmopolymers and osmagent occurs swells as fluid is imbibed, leading to drug release (col 8, ln 20 – 25). Poly(alkylene) oxides, poly(carboxymethyl celluloses), poly (alkali carboxymethyl celluloses) or hydroxypropylalkyl celluloses such as HPMC can be used as the hydrophilic polymer (col 13, ln 5 – 32). Polymers that swell will not dissolve in water or an aqueous fluid. Carbohydrates such as maltodextrin can be used alone or in combination with other osmagents (col 13, ln 33 – 37). In Example 4B (col 22, ln 24 – 50), the drug layer comprises a pharmaceutically acceptable amount of reboxeinate methanesulfonate, maltodextrin and stearic acid, a lubricant. The push layer comprises polyethylene oxide, which reads on a hydrophilic polymer that is sustained release carrier (see claim 71 of the instant application), hydroxypropyl methyl cellulose 2910 (HPMC, a water insoluble or partially water insoluble cellulose) and magnesium stearate, a lubricant.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate the osmagent maltodextrin into the drug delivery compositions of Shell et al. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because both Shell et al. and Seroff et al. teach drug delivery devices that are driven by

the imbibition of water from the external environment into the drug delivery device. Shell et al. discloses that such drug delivery devices need not have the push layer and drug layer configuration as in Seroff but instead all of the components can be combined into a single composition. While Shell et al. does not explicitly state that the composition is homogenous, mixing of the various ingredients present in the formulation to homogeneity will decrease the variability in drug dosage amount from one dosage form to the next.

The amount of swelling, determined by the particular polymer(s) and other osmagents such as maltodextrin present in the dosage form will determine the rate and amount of swelling of the dosage form and thus the release rate of the drug from the dosage form. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results of the desired release rate for the particular drug, such as metformin, being released from a given dosage form. The combination of swellable polymers is taught by the formulations of Seroff and the combination of gums and celluloses is taught as a particularly advantageous combination by Shell et al. to provide more control over the release of drug. The inclusion of maltodextrin also acts to control the imbibition of water and thus control of the drug release rate.

In regards to the claim limitation “wherein said water insoluble or partially water insoluble cellulose in combination with maltodextrin further effect the release of the drug”, this is a property of the dosage form. There is no evidence currently on the record that a monolithic, single layer drug delivery form like that taught by Shell et al. will not have this property. “As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith.” **MPEP 2113** It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

5. Claims 48 and 67 – 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shell et al. in view of Seroff et al. as applied to claims 38, 40 – 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 above, and further in view of Tobyn et al. (Intl J Pharm 1998).

As discussed in greater detail above, Shell et al. discloses a drug delivery form that operates based on the principle of water imbibition by the dosage form, leading to drug release. The dosage form comprises a single layer and maltodextrin can be included in such a dosage form as an osmagent with different water swelling properties

that the water-swelling polymers, leading to an altered swelling and thus release profile. Shell et al. disclose microcrystalline cellulose as a water-swellable polymer that can be present in the dosage form.

Neither reference discloses the use of silicified microcrystalline cellulose (SMCC).

Tobyn et al. discloses the MCC is widely used as a filler and binder for wet granulation, direct compression tabletting and a filler for hard gelatin capsules (p 183, col 1, ¶1) and it has been rated as the most useful filler for direct compression tabletting (p 183, col 2, ¶1). While MCC is very useful, SMCC possesses a number of advantages in terms of powder flow, tablet strength, lubricant sensitivity and wet granulation (p 184, col 2, ¶ 1).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate SMCC in place of MCC into the formulations of Shell et al. and Seroff et al. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because Tobyn et al. teaches the improved behavior of SMCC when formulations are prepared.

## ***Conclusion***

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NISSA WESTERBERG whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nissa M Westerberg/
Primary Examiner, Art Unit 1618